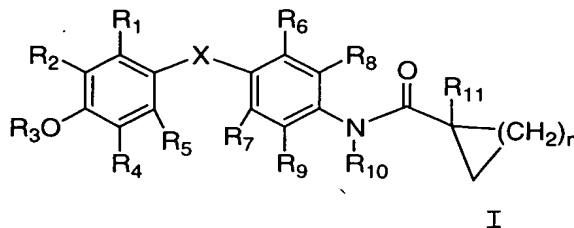


What is claimed is:

1. A compound of formula I



5

wherein

X is selected from oxygen (-O-), selenium (-Se-), sulfur (-S-), sulfenyl (SO), sulfonyl (SO₂), carbonyl (-CO), methylene (-CH₂-) and -NH-;

R₁ is selected from hydrogen, halogen, CF₃ and C₁ to C₆ alkyl;

R₂ is selected from halogen, CF₃, C₁ to C₆ alkyl, C₂ to C₆ alkenyl, C₂ to C₆ alkynyl, C₃ to C₇ cycloalkyl, C₄ to C₇ cycloalkenyl, aryl, heteroaryl, alkoxy, aryloxy, heteroaryloxy, arylalkoxy, cycloalkoxy, N(R₁₂)COR₁₃, CO(NR₁₂R₁₃), N(R₁₂)SO₂R₁₃, SO₂(NR₁₂R₁₃), SR₁₄, SOR₁₄, SO₂R₁₄, COR₁₄, CR₁₂(OR₅)R₁₃ and CH₂NR₁₂R₁₃;

R₃ is selected from hydrogen, alkyl, benzyl, aroyl and alkanoyl;

R₄ and R₅ are each independently selected from hydrogen, halogen and alkyl;

R₆ and R₇ are each independently selected hydrogen, halogen, cyano, C₁ to C₄ alkyl and C₃ to C₆ cycloalkyl, where at least one of R₆ and R₇ is other than hydrogen;

R₈ and R₉ are each independently selected from hydrogen, halogen, alkoxy, hydroxy, cyano, CF₃ and alkyl;

R₁₀ is hydrogen or alkyl;

R₁₁ is CO₂R₁₃ or tetrazole;

R₁₂ and R₁₃ for each occurrence are each independently selected from hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

30

R_{14} is selected from alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl; and

n is an integer from 1 to 4,

including all prodrugs, stereoisomers and
5 pharmaceutically acceptable salts thereof.

2. The compound as defined in Claim 1 wherein X is oxygen.

10 3. The compound as defined in Claim 2 wherein

R_1 is hydrogen;

R_2 is C_1 to C_6 alkyl or C_3 to C_7 cycloalkyl;

R_3 is hydrogen;

R_4 is hydrogen, halogen or alkyl;

15 R_5 is hydrogen;

R_6 and R_7 are each independently bromo, chloro or C_1 to C_4 alkyl;

R_8 is hydrogen, halogen or alkyl;

R_9 is hydrogen or halogen;

20 R_{10} is hydrogen;

R_{11} is carboxyl; and

n is 2 or 3.

4. The compound as defined in Claim 3 wherein R_2 is
25 isopropyl.

5. The compound as defined in Claim 2 wherein

R_1 is hydrogen;

R_2 is isopropyl;

30 R_3 is hydrogen;

R_4 is chloro or C_1 to C_4 alkyl;

R_5 is hydrogen;

R_6 and R_7 are each independently bromo, chloro or
methyl;

35 R_8 is hydrogen, chloro or C_1 to C_4 alkyl;

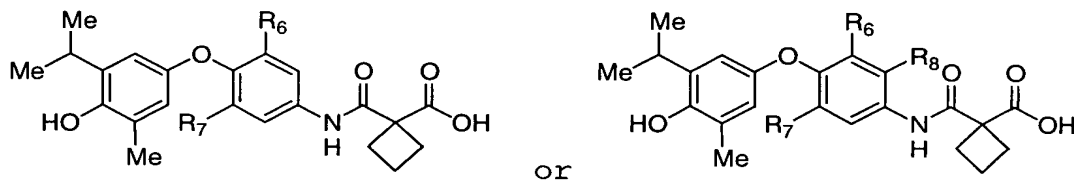
R₉ is hydrogen;
R₁₀ is hydrogen;
R₁₁ is carboxyl; and
n is 2.

5

6. The compound as defined in Claim 2 wherein

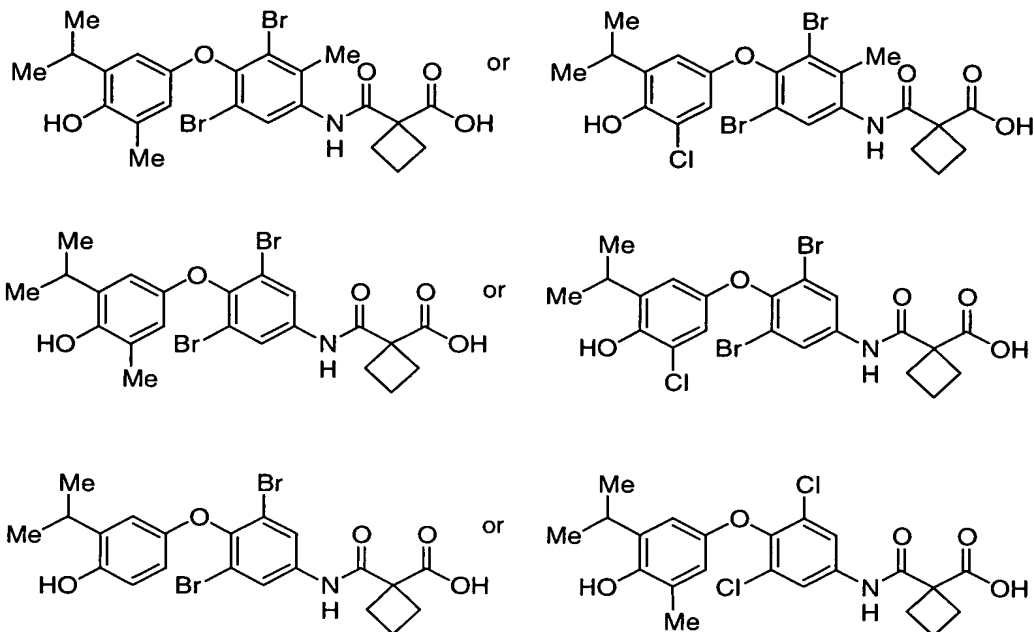
R₁ is hydrogen;
R₂ is isopropyl;
R₃ is hydrogen;
10 R₄ is chloro or methyl;
R₅ is hydrogen;
R₆ and R₇ are bromo;
R₈ is hydrogen or methyl;
R₉ is hydrogen;
15 R₁₀ is hydrogen;
R₁₁ is carboxyl; and
n is 2.

20 7. The compound as defined in Claim 1 having the structure



or an alkyl ester thereof.

8. The compound as defined in Claim 1 having the structure



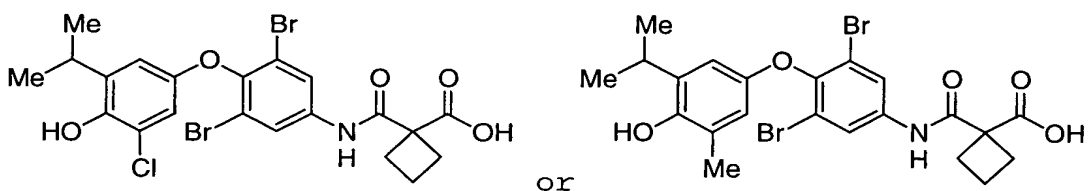
5

or

or an alkyl ester thereof.

9. The compound as defined in Claim 1 having the structure:

10



15

10. A pharmaceutical composition comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier therefor.

11. The pharmaceutical composition of claim 10 further comprising at least one additional therapeutic agent

selected from other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, 5 cardiac glycosides, cholesterol/lipid lowering agents, appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

12. The pharmaceutical composition of claim 11
10 wherein said additional therapeutic agent is an antidiabetic agent selected from a biguanide, a glucosidase inhibitor, a meglitinide, a sulfonylurea, a thiazolidinedione, a PPAR-alpha agonist, a PPAR-gamma agonist, a PPAR alpha/gamma dual agonist, an SGLT2 inhibitor, a glycogen phosphorylase
15 inhibitor, an aP2 inhibitor, a glucagon-like peptide-1 (GLP-1), a dipeptidyl peptidase IV inhibitor and insulin.

13. The pharmaceutical composition of claim 11
wherein said additional therapeutic agent is an antidiabetic
20 agent selected from metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, troglitazone, pioglitazone, englitazone, darglitazone, rosiglitazone and insulin.

25 14. The pharmaceutical composition of claim 11
wherein said additional therapeutic agent is an anti-obesity agent selected from an aP2 inhibitor, a PPAR gamma antagonist, a PPAR delta agonist, a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin reuptake inhibitor,
30 a cannabinoid-1 receptor antagonist and an anorectic agent.

15. The pharmaceutical composition of claim 11
wherein said additional therapeutic agent is a hypolipidemic agent selected from a thiazolidinedione, an MTP inhibitor, a
35 squalene synthetase inhibitor, an HMG CoA reductase

inhibitor, a fibric acid derivative, an ACAT inhibitor, a cholesterol absorption inhibitor, an ileal Na⁺/bile cotransporter inhibitor, a bile acid sequestrant and a nicotinic acid or a derivative thereof.

5

16. A method for preventing, inhibiting or treating a disease associated with metabolic dysfunction, or which is dependent on the expression of a T₃ regulated gene, which comprises administering to a mammalian patient in need of
10 treatment a therapeutically effective amount of a compound as defined in claim 1.

17. A method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis,
15 depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disorder or disease,
20 which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

18. The method according to claim 17 wherein the skin
25 disorder or disease is dermal atrophy, post surgical bruising caused by laser resurfacing, keloids, stria, cellulite, roughened skin, actinic skin damage, lichen planus, ichthyosis, acne, psoriasis, Dernier's disease, eczema, atopic dermatitis, chloracne, pityriasis or skin
30 scarring.

19. The method according to claim 17 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional
35 therapeutic agent selected from other compounds of formula

I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid
5 lowering agents, appetite suppressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

20. A method of treating or delaying the progression or
10 onset of a skin disorder or disease which comprises administering to a mammalian patient a therapeutically effective amount of a compound as defined in claim 1 in combination with a retinoid or a vitamin D analog.

15 21. A method for treating or delaying the progression or onset of obesity which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

20 22. A method according to claim 21 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from an anti-obesity agent and an appetite suppressant.

25 23. A method according to claim 22 wherein said anti-obesity agent is selected from aP2 inhibitors, PPAR gamma antagonists, PPAR delta agonists, beta 3 adrenergic agonists, lipase inhibitors, serotonin (and dopamine)
30 reuptake inhibitors, cannabinoid-1 receptor antagonists, other thyroid receptor agents and anorectic agents.

24. A pharmaceutical composition which functions as a selective agonist of the thyroid hormone receptor comprising
35 a compound as defined in claim 1.